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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/986,568	12/05/1997	JEAN-FRANCOIS BACH	040388/0110	5102

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STEPHEN A BENT
FOLEY & LARDNER
3000 K STREET NW SUITE 500
PO BOX 25696
WASHINGTON, DC 200078696

EXAMINER
SAUNDERS, DAVID A

ART UNIT	PAPER NUMBER
1644	27

DATE MAILED: 06/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 3/8/02

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-2, 4-7, 9-13, 16-18 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 1-2, 4-7, 9-13, 16-18 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

-SEE OFFICE ACTION ON THE FOLLOWING PAGES-

The amendment of 3/8/02 has been entered. Claims 1-2, 4-7, 9-13 and 16-18 are pending. Prosecution is reopened, and the clams are newly rejected herein below.

Claims 1, 6, 9-13 and 17-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant did not posses the genus of "anti-CD3 active compounds".

The only examples of such compounds that applicant has given or suggested are antibodies to CD3 (or compounds that would also be encompassed by antibodies such as antibody fragments, humanized antibodies, etc.). Applicant has directed the reader to no other genre of compounds, nor could one readily envision other kinds of compounds such as lipids, carbohydrates, or non-Immunoglobulin polypeptides that would be "anti-CD3 active". Applicant has disclosed no other type of compound which, like an anti-CD3 antibody, is capable of binding to CD3 in a ligand-receptor manner. Applicant has failed to describe any type of common structure that such a genus of compounds must have in order to bind to the CD3 antigen. Applicant has thus failed to adequately describe the genus of "anti-CD3 active" members, except for those members which are anti- CD3 antibodies.

Claims 1-2, 4-7, 9-13 and 16-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant has not enabled the treatment of established autoimmune disease in humans.

Applicant's disclosure has only exemplified NOD strain mice, and it would be unpredictable as to whether or not such treatments would also be efficacious in humans. Applicant and co-authors have clearly admitted that the same results obtained in NOD mice (as shown in the 102(b) reference of Chatenoud et al) would need to be "confirmed" in humans and that such a therapy is only a "possibility". See page 127, col. 2, last full para.

Claims 1-2, 4-6, 9-13 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chatenoud et al (PNAS, 91, 123-127, 1994).

The article of Chatenoud et al has been applied as a 102 reference by the BPAI (Decision of 1/9/02). While applicant's amendment of 3/8/02 has overcome anticipation, by inserting "human" in lieu of "mammal", the issue of obviousness remains. Clearly, the authors suggest that treatments like those disclosed for NOD mice should be applied to humans with diabetes. See page 127, col.2, last full para.

Presently claim 6 is added to those previously rejected under 102, because Chatenoud et al teach the limitation of providing a purified, endotoxin free anti-CD3 antibody for in vivo treatment. See page 123, col. 2, third full para.

Regarding claims 10-12, which recite well known autoimmune diseases other than diabetes, the treatment of any of these would have been obvious because the anti-CD3 antibody of Chatenoud et al modulates the CD3/TCR cell surface receptor complex, irrespective of the antigenic specificity of the TCR. Hence one would have expected that modulation of the CD3/TCR complex, by administration of anti-CD3, would likewise be efficacious in treating any established autoimmune disease in which the TCR recognizes an autoantigen other than that involved in diabetes.

Regarding claims 17-18, it is noted that Chatenoud et al used doses of 5ug/day for mice. Taking the typical weight of a human to be 70kg and the typical weight of a mouse to be 20g (.02kg), one of ordinary skill would have expected that multiplying the dose given to mice by a factor of 70/.02 (or 3500) would provide a dose appropriate for humans. That is, 5ug/day X 3,500 gives a dose of 17.5mg/day for humans. This clearly falls within the range recited in claim 17, and it falls within a factor of 2 of the range recited in claim 18, which factor is considered good enough for stating obviousness in biological systems which do not typically operate within only a narrow range of parameters.

Claims 1, 4 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chatenoud et al in view of Gussow et al (Meth. Enzymol., 203, 99, 1991).

Chatenoud et al have been cited supra against base claims 1 and 4. Chatenoud et al do not teach use of a mouse or of an humanized antibody in their treatment method. Apparently they used a hamster antibody, rather than a mouse antibody because, to prepare an antibody against mouse CD3, an antibody prepared in another immunized animal species was required. However, in the case of treating humans, as now claimed, one would have expected to use anti-CD3 antibodies prepared from conventional hosts. Gussow et al teach (page 99) that, to the date of their reference, most of the monoclonal antibodies of potential therapeutic value were of mouse origin. They also teach that, in order to avoid HAMA responses, one would be motivated to provide humanized variants of mouse monoclonal antibodies (page 99). Hence, if one were willing to take a step backward in the art, it would have been obvious to treat humans with mouse antibodies to CD3, or , if one wanted to avoid HAMA responses, it would have been obvious to treat humans with humanized mouse monoclonal antibodies to CD3 when applying

the method of Chatenoud et al to the treatment of humans. Note that Gussow et al do not limit their motivation for providing humanized monoclonal antibodies to those of any particular antigenic specificity. Hence, one would have been motivated to humanize anti-CD3 monoclonal antibodies as much as one would have been motivated to humanize antibodies against any other antigen of interest for in vivo diagnosis or therapy in humans.

In summary, the above 112 enablement and 103 rejections are made of the basis that either 1) applicant's invention of treating humans may have been enabled but obvious, or 2) applicant's invention of treating humans was obvious to try, but the outcome was unpredictable (requiring more than routine experimentation in order to reduce to actual practice in humans). Applicant is thus stuck with either holding to position 1) or 2) and cannot argue that the invention was both enabled and unobvious.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A Saunders, PhD whose telephone number is 703-308-3976. The examiner can normally be reached on Mon-Thu from 8:00 to 5:30. The examiner can also be reached on alternate .

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Typed 6/10/02

BRUCE R. WESTERINK, DIRECTOR
TECHNOLOGY CENTER 1600

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182 1644